19 June 2006

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ROBUST SUMMARY FOR SEC-BUTYL UREA

Summary

SBU is an odorless white crystalline solid with a measured sublimation point of 171°C, and an estimated boiling point of 224.95°C. Sec-butyl urea has a specific gravity of 0.25-0.28, and an estimated log Kow of 0.31. Sec-butyl urea has a water solubility value of 4 wt% at 20°C, and a vapor pressure of 1.40×10^{-3} Pa at 25°C.

Modeled data rank sec-butyl urea as being of low environmental concern for stewardship and regulatory action. This ranking results from a low persistence and bioaccumulation score using the standard EPA emissions scenario of equal emissions to air, water, and soil. The predicted half-life in sediment of 140 days, indicates moderate persistence in this environmental compartment, but the estimated distribution based on Level III fugacity modeling predicts that sec-butyl urea will not partition into this compartment under tested release scenarios. Water and soil are predicted to be the major environmental compartments into which sec-butyl urea will partition. Estimated hydrolysis rates in water are slow. A ready biodegradability test following OECD Guideline 301 was run. Sec-butyl urea reached a maximum biodegradability of 14% by test day 28, and was considered not "ready biodegradable."

ECOSAR (Meylan and Howard, 1999) was used to estimate the missing aquatic toxicity data for SBU to fish, *Daphnia* (planktonic freshwater crustaceans), and algae. Based on the fact that sec-butyl urea is produced at only one DuPont site as an isolated intermediate[1] and ECOSAR predictions of an estimated 96-hour LC_{50} in fish of 1806 mg/L, an estimated 48-hour EC_{50} in *Daphnia* of 3184 mg/L, and an estimated 96-hour EC_{50} in green algae of 3339 mg/L SBU would be of low concern for toxicity to aquatic organisms. Substantiating these results are measured data and ECOSAR results for a structurally related compound, isobutylidene diurea (IBDU; CAS# 6104-30-9). Measured aquatic toxicity data for this analog compound, as well as data estimated using ECOSAR, indicate that it is of low concern for toxicity to aquatic organisms. The difference in toxicity is related solely to the Kow of the compound. Given the agreement between ECOSAR and actual test data for the analog compound, and the low observed toxicity of the analog and predicted toxicity for sec-butyl urea, no additional aquatic testing is warranted.

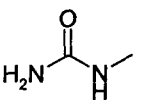
[1]As defined by EPA guidance, an isolated intermediate is one in which there is controlled transport, i.e. to a limited number of locations within the same company or second parties that use the chemical in a controlled way as an intermediate with a well known technology.

Compound	Algae, 96-hr EC_{50}	Daphnid, 48-hr EC_{50}	Fish, 96-hr LC_{50}
Sec-butyl urea	1806 mg/L[a]	3184 mg/L[a]	3339 mg/L[a]
Isobutylidene diurea	156,000 mg/L[b] >500 mg/L*	309,000 mg/L[b] >1000 mg/L*	372,000 mg/L[b] >1000 mg/L*
* Measured data. [a] Log_{10} Kow of 0.31 used for modeling. [b] Log_{10} Kow of −1.68 used for modeling.			

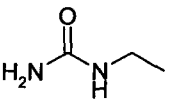
Sec-butyl urea (SBU) has very low acute oral toxicity with an ALD of 7500 mg/kg in rats. SBU was a moderate eye irritant, producing temporary corneal injury, iritic congestion, and conjunctivitis when tested in rabbit eyes.

There is no developmental toxicity study available for SBU. Although the quantitative structure toxicity relationship (QSTR) model TOPKAT predicts that SBU would be a developmental toxicant, literature on a closely related material suggests that SBU would not be a developmental toxicant. When using such QSTR models, it is important to examine the training set of compounds from which the model is derived. The majority of the training set of structures the TOPKAT model is based upon thioureas that are known developmental toxicants. One possible mechanism for the toxicity of thioureas is the formation of reactive sulfonyl metabolites during the oxidative desulfuration reaction. Under this mechanism, the corresponding ureas are not reactive, but are detoxification products of the thioureas. Therefore, using thioureas as the training set to build the QSTR model for the ureas is scientifically unsound and invalid.

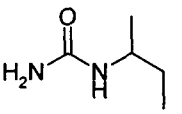
A study of the teratogenic effects of *N*-alkylureas (e.g., 1-methylurea, 1-ethylurea) found they are not teratogens, while their corresponding thioureas (1-methylthiourea and 1-ethylthiourea) are teratogenic (Teramoto et al., 1981). Using the closest neighbor analogy, we strongly believe that it is unlikely that SBU is a teratogen.



1-methylurea
(not a teratogen)



1 -ethylurea
(not a tetatogen)



sec-butylurea (SBU)

Based on the above scientific justification and using the scientific rationale consistent with the procedures described in the EPA Office of Pollution Prevention and Toxin technical document "The use of Structure-Activity Relationship (SAR) in the High Production Volume Chemical Challenge Program," no additional testing for developmental toxicity is necessary based on the following:

- **There is limited potential for exposure to SBU in quantities sufficient to produce effects**

SBU is a solid substance; the likelihood of exposure by the inhalation or dermal absorption route is negligible. It has very low toxicity by the oral route (rat oral ALD >7500 mg/kg). Information is presented that the potential for human contact in any substantial amount is quite low.

- **Alkyureas should not be grouped with alkylthioureas in the development of structure-toxicity activity relationship**

Teramoto et al., 1981 reported the relationship between the molecular structure of *N*-alkylureas and *N*-alkylthioureas and their teratogenic properties. Single maximum tolerated doses of 2000 mg/kg urea, methylurea, or ethylurea were given to pregnant rats on Day-12 of gestation. There were no significant differences from controls in mean number of implants, mean number of live fetuses, percent fetal resorptions, mean fetal weight, or percent malformed fetuses. In contrast, a number of these parameters were affected by the corresponding thioureas.

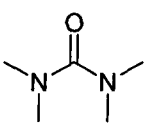
Two important conclusions were reached:

1) The thiourea (C=S) moiety was essential for teratogenic potency potential.

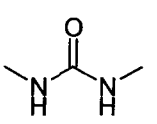
"There is one structural similarity between mono-alkylated thioureas and ETU which is essential for teratogenic potency. The C=S group is essential to mono-alklyated thioureas for manifesting teratogenic effects. Replacement of the C=S group with C=O (i.e., 1-methylurea or 1-ethylurea) resulted in the loss of teratogenicity."

2) The developmental toxicity of urea is related to the increasing number of methyl groups attached.

Results from Teramoto's study are in agreement with the results reported by Von Kreybig et al., 1969, that "....teratogenic activity is enhanced by the increasing number of methyl group attached... 1,1,3,3-tetramethylurea , but not 1,3-dimethylurea, was teratogenic in rats...1,1,3,3-tetrametylurea is a strong teratogen toward the mouse fetus, where 1,3-dimethylurea was weak...."



1,1,3,3-tetramethylurea



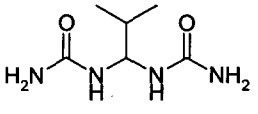
1,3-dimethylurea

The teratogenic effects of the thioureas and methylated ureas are different. "...Thioureas affect CNS whereas methylated urea malformations are detected in the palate, tail, and extremities..." Furthermore, the effect observed with the ureas decreases with the increasing alkyl moiety..."

These two research findings support the conclusion that *sec*-butylurea is unlikely to be a teratogen/developmental toxicant, based on structural similarity to methylurea, ethylurea, and 1,3-dimethylurea. In view of the above observations, it is unlikely that SBU will exhibit the CNS or structural malformation effects exhibited by both the thioureas and methylated ureas.

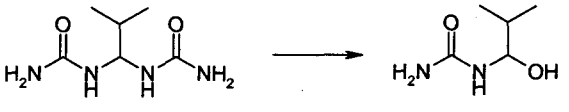
- **Studies with structurally related alkyl ureas show no developmental toxicity**

In addition to the study above in which rats were given large single doses during pregnancy, a traditional rat developmental study is available on isobutylidenediurea (IBDU, CAS #6104-30-9). Wistar rats were given 0, 100, 400, or 1000 mg/kg IBDU in aqueous carboxymethyl cellulose suspension during days 6-15 of gestation (Hellwig, 1997; see also Section 6.3). There were no substance-related effects in dams (including body weight, body weight gain, food consumption, clinical signs of toxicity, or reproductive data) at any dose level tested. There was no increased incidence of fetal malformations, variations, or retardations at any dose level tested. Therefore, the no effect level for the maternal and developing organism was 1000 mg/kg/day, the highest dose tested. IBDU was not a developmental toxicant in rats.



N, N"-(Isobutylidene)bisurea
N, N" -(Isobutylidene)diurea
N,N"-(2-Methylpropylidene)bisurea
CAS# 6104-30-9

N,N-(isobutylidene)diurea (IBDU) is a diurea that would be metabolized *in vivo* via an *N*-dealkylation reaction to yield 1-hydroxy isobutylurea (IBU-OH), a close structural analog of SBU.



IBDU IBU-OH

The close structural similarity between SBU and IBU also support the conclusion that SBU will be negative under same test condition as IBDU.

IBU SBU

IBDU/IBU can be considered as a suitable surrogate to testing SBU.

Related alkyl ureas that have been evaluated are not developmental toxins. One of the alkyl ureas already evaluated, and found not to be developmentally toxic is IBDU.

Lastly, reliance on existing studies would prevent unnecessary wastage of animals. Therefore, it can be concluded, based on existing literature, that SBU is unlikely to be developmentally toxic.

Therefore, DuPont proposes that no additional developmental toxicity testing is necessary for SBU based on available data for a related material. The physical nature of the material (solid and high water solubility) makes inhalation and dermal exposure unlikely. Oral exposure is not expected, since SBU is an industrial product not a consumer product.

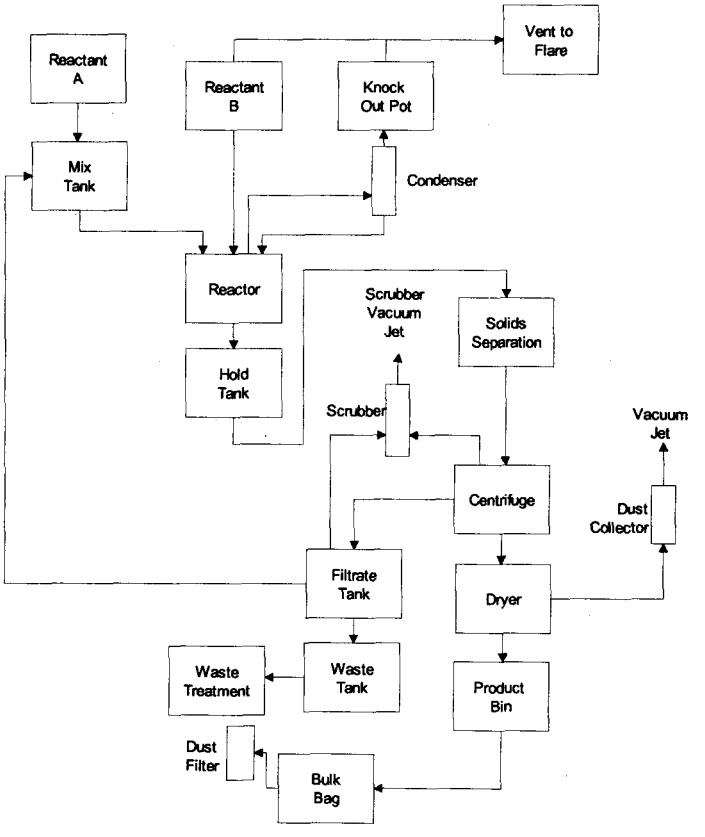
SBU was negative in a bacterial reverse mutation assay and negative in an *in vitro* chromosome aberration test in human peripheral blood lymphocytes.

As described below, the test material is an isolated intermediate; therefore, repeated dose and reproductive toxicity data are not required.

Human Exposure

Sec-butyl urea, a white crystalline solid, is a chemical intermediate used in the production of a FIFRA registered herbicide. Sec-butyl urea (SBU) is manufactured at one DuPont facility (Belle Plant, WV), and is shipped overseas by bulk bag (333 kgs) to only one customer. 100% of the sec-butyl urea is sold into this application.

A process flow diagram for the DuPont SBU process is shown below.



SBU is made at the DuPont Belle Plant on a campaign basis (lasting several months) each year, as an isolated intermediate, with controlled transport to one other location within a second party that uses the chemical in a controlled way as an intermediate. The raw materials are mixed and reacted, then the product is filtered and dried. SBU is packed in bulk bags, placed on a cardboard sheet on pallets, and loaded in overseas shipping containers. There is no mixing of materials in the shipping containers, — they only contain SBU. Process wastes and cleanup waste from the manufacture of SBU are treated at the on-site biological treatment plant, which is covered under a NPDES permit with the state of West Virginia.

Dust is contained in the SBU production system in the following ways. The dust produced during drying is contained in a dust collector and returned to the dryer. The dryer is discharged into a bin, which is vented through a vent sock filter. After each dryer batch is discharged, the dryer dump valve is cleaned. One to two SBU bulk bags are filled from each dryer batch. The bulk bag inlet is fitted over the charge nozzle. The bags are vented through a vent sock to capture dust during filling. Then the bag inlet is removed from the charge nozzle and the bag is closed. Cleaning the dryer door is performed approximately 5 times per shift, and 5 to 10 SBU bags are produced per shift. Due to the generally needle-like structure of the SBU crystals, SBU is less dusty than some materials. Potential for worker exposure to SBU during process operation and filling SBU bulk bags is characterized by the sampling results discussed at the end of this section.

Workers wear PPE as protection from leaks and spills when breaking lines or entering equipment for maintenance. This PPE consists of dust resistant gloves and goggles for breaking into lines. Equipment is normally wet-cleaned prior to entering equipment. However, if excessive dust is generated, a NIOSH approved air purifying respirator with particulate filters is worn.

The sites can have from 2 to 5 personnel working (construction, contractor, and plant employees). The areas where the substance is manufactured will have from 1 to 2 workers during normal operations and 4 to 10 people during a shutdown. Equipment is wet cleaned so that dust generation is minimized. The site that produces SBU has effective safety, health and environmental practices and procedures in addition to engineering controls, environmental controls, and personal protective equipment to control exposure. Adequate safety equipment, such as safety showers, eyewash fountains, and washing facilities, are available in the event of an occupational exposure. Individuals handling SBU should avoid contact with eyes, skin, or clothing, should not breathe dust, and should wash thoroughly after handling.

The only customer for SBU is located outside the US in Israel. This customer produced SBU from their own process for many years. SBU is stored by the customer in the bulk bags until charged to the reactor through a charge bin. All charging units are connected to a DCE dust collector. The dust collector filters are replaced between campaigns. DuPont conducted a contamination prevention audit at the customer's facility, and found that the customer's handling of the SBU included adequate controls.

Air monitoring has been conducted for the loading area of the DuPont Belle facility (SBU) and results are shown in the table below. LOGAN (lognormal analysis) is a computerized statistical method for characterizing occupational exposures to chemicals, noise, and other environmental hazards. LOGAN uses sequential collection of data and makes decisions on the minimum amount of data. It helps make cost-effective, accurate decisions that ensure a healthy workplace. LOGAN uses inferential statistics to estimate the true workplace conditions, in the same way that public polling estimates opinions by sampling a representative percentage of the public. LOGAN is designed to limit the risk of employee occupational overexposure to less than 5%.

Although a DuPont Acceptable Exposure Limit (AEL) has not been established for sec-butyl urea, the site uses a 10 mg/m^3, total dust, exposure limit for SBU based on an analogy to tertiary-Butylurea. The DuPont Acceptable Exposure Limit (AEL) for tertiary-Butylurea is 10 mg/m^3, total dust. Air monitoring has been conducted to characterize employee exposure to secondary-Butylurea (SBU) and results are shown in the table below. All measured concentrations are well below the 10 mg/m^3 exposure limit, and the conclusion of the Logan analysis was "Acceptable". Results shown in the table below characterize exposure for those who perform SBU production job, including filling SBU bags and cleaning the dryer dump valve.

Exposure Data:

Job Sampled	No. of Results	Average (mg/m^3)	Minimum (mg/m^3)	Maximum (mg/m^3)
DuPont Manufacturing Site Workers (full shift)	**18***	**0.129**	**<0.1**	**0.4**

* For time period 1998-2003

References for Summary:

Hellwig, J. et al. (1997). Food Chem. Toxicol., 35:677-681.

Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210 (submitted for publication).

Teramoto, S. et al. (1981). Teratology, 23:335-342.

Von Kreybig, T. et al. (1969). Arzneim. Forsch., 19:1073-1076.

19 June 2006

TEST PLAN FOR SEC-BUTYL UREA

Sec-butyl urea CAS No. 689-11-2	Data Available	Data Acceptable	Testing Required
Study	**Y/N**	**Y/N**	**Y/N**
PHYSICAL/CHEMICAL CHARACTERISTICS			
Melting Point	Y	Y	N
Boiling Point	Y	Y	N
Vapor Pressure	Y	Y	N
Partition Coefficient	Y	Y	N
Water Solubility	Y	Y	N
ENVIRONMENTAL FATE			
Photodegradation	Y	Y	N
Stability in Water	Y	Y	N
Transport (Fugacity)	Y	Y	N
Biodegradation	Y	Y	N
ECOTOXICITY			
Acute Toxicity to Fish	Y[1]	Y	N
Acute Toxicity to Invertebrates	Y[1]	Y	N
Acute Toxicity to Aquatic Plants	Y[1]	Y	N
MAMMALIAN TOXICITY			
Acute Toxicity	Y	Y	N
Repeated Dose Toxicity	N/A	N/A	N/A
Developmental Toxicity	Y[2]	Y	N
Reproductive Toxicity	N/A	N/A	N/A
Genetic Toxicity Gene Mutations	Y	Y	N
Genetic Toxicity Chromosomal Aberrations	Y	Y	N

[1]Data for a related material, isobutylidene diurea, are available.
[2]Data for related materials, isobutylidene diurea, urea, methylurea, and ethylurea, are available.

I U C L I D

Data Set

Existing Chemical	:	ID: 689-11-2
CAS No.	:	689-11-2
EINECS Name	:	sec-butylurea
EC No.	:	211-709-1
Molecular Formula	:	C5H12N2O

Producer related part

Company	:	E. I. du Pont de Nemours and Company
Creation date	:	27.12.2005

Substance related part

Company	:	E. I. du Pont de Nemours and Company
Creation date	:	27.12.2005
Status	:	
Memo	:	
Printing date	:	19.06.2006
Revision date	:	
Date of last update	:	17.03.2006
Number of pages	:	34
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1. General Information

Id 689-11-2
Date 19.06.2006

1.0.1 APPLICANT AND COMPANY INFORMATION

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

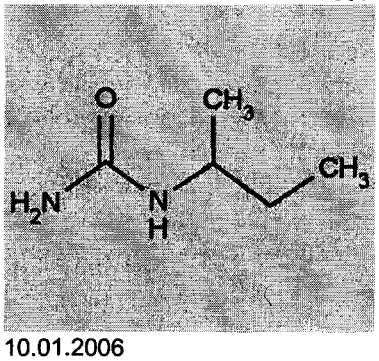
1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name : Urea, (1-methylpropyl)-
Smiles Code :
Molecular formula :
Molecular weight : 116.16
Petrol class :

27.12.2005

1.1.1 GENERAL SUBSTANCE INFORMATION

Attached document : sec-Butylurea picture.bmp



10.01.2006

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

N-sec-butylurea

27.12.2005

Sec-butylurea

27.12.2005

Secondary butylurea

27.12.2005

Urea, 1-sec-butyl-

27.12.2005

Urea, sec-butyl-

27.12.2005

1.3 IMPURITIES

1.4 ADDITIVES

1.5 TOTAL QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Sublimation	:	yes
Method	:	
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Reliability: Not assignable because limited study information was available.
Result	:	Sublimation at 171°C

04.01.2006 (7) (8)

2.2 BOILING POINT

Value	:	225 °C at 1018 hPa
Decomposition	:	
Method	:	other
Year	:	
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Modeled. MPBPWIN, v. 1.4 module of EPIWIN 3.05 (Syracuse Research Corporation). MPBPWIN estimates the normal boiling point using an adaptation of the Stein and Brown (1994) method, which is an extension and refinement of the Joback method (Joback, 1982; Reid et al., 1987).
Remark	:	Reliability: Estimated value based on accepted model.

04.01.2006 (17) (28) (32)

2.3 DENSITY

Type	:	relative density
Value	:	.25 - .28 at °C
Method	:	
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Reliability: Not assignable because limited study information was available.

27.12.2005 (8)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value	:	.000014 hPa at 25 °C
Decomposition	:	
Method	:	OECD Guide-line 104 "Vapour Pressure Curve"
Year	:	2005
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The study was patterned after the following guidelines:

OECD Guideline 104 and

US EPA OPPTS 830.7950.

Preliminary and definitive tests were performed. The results of the preliminary test were reported as the vapor pressure at an elevated temperature. The definitive test was thus performed to show the vapor pressure at 25°C. The experiment was conducted at 2 different flow rates of nitrogen to show that the test substance had saturated the nitrogen gas. The flow rate of all systems was adjusted to 8 mL/min and measured with a digital flow meter. Flow rates were confirmed and adjusted several times throughout the study. The definitive test duration was chosen based on the amount of test material collected in the preliminary test, and was approximately 167 hours (6.96 days). A 10 mL/min definitive test was conducted exactly as described for the 8 mL/min definitive test, with the exception that the flow of nitrogen through the saturator columns was 10 mL/min.

Remark : Reliability: High because a scientifically defensible or guideline method was used.

Result : The test substance was determined to have a vapor pressure of .000173 hPa (1.73E-02 Pa; 1.30E-04 torr) at 50°C and .0000140 hPa 1.40E-03 Pa; 1.05E-05 torr) at 25°C. The vapor pressure was determined to be 8.03E-04 Pa (6.02E-04 torr) at 20°C based on extrapolation of the data at 25°C and 50°C.

Test substance : sec-Butyl urea, purity 99.4%

Flag : Critical study for SIDS endpoint

16.01.2006 (12)

2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water
Log pow : .31 at 25 °C
pH value :
Method :
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Modeled. KOWWIN, v. 1.66, module of EPIWIN 3.05 (Syracuse Research Corporation). KOWWIN uses "fragment constant" methodologies to predict log P. In a "fragment constant" method, a structure is divided into fragments (atom or larger functional groups) and coefficient values of each fragment or group are summed together to yield the log P estimate.

Remark : Reliability: Estimated value based on accepted model.

04.01.2006 (24)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in : Water
Value : 4 other: WT% at 20 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :

Method	:	
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Reliability: Not assignable because limited study information was available.
27.12.2005		(8)
Solubility in	:	Water
Value	:	10 other: WT% at 60 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Reliability: Not assignable because limited study information was available.
27.12.2005		(8)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

Result	:	other
Method	:	other
Year	:	1995
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	A Hartmann Dust Tube was used to determine the lower explosive limit (LEL), limiting oxygen concentration (LOC), and minimum ignition energy (MIE). A weighed sample was placed into a cup at the base of a sealed stainless steel tube. A continuous AC arc was energized between 2 tungsten electrodes in the tube as a pulse of air dispersed the sample into a cloud. If the sample concentration was above the LEL, defined as the lowest dust concentration sufficient for sustained flame propagation, the arc would cause the material to deflagrate and the resulting pressure increase would be detected by a pressure transducer in the top of the tube. Pressure/time and rate/time measurements were recorded. LEL was reported as the highest dust concentration resulting in a "NO GO" (pressure increase <1 psig over initial dispersion pressure). The LOC, defined as the highest oxygen concentration permissible to prevent combustion for any dust concentration, was determined with a

modified version of the above procedure. Ignition was attempted on dust samples of various concentrations that were dispersed by oxygen/nitrogen mixtures of known compositions. The sample was tested at decreasing oxygen levels until a point was reached where no combustion events were observed (pressure increase <1 psig over initial dispersion pressure) for any of the concentrations tested. This level was reported as the LOC.

The test method for MIE involved subjecting dust clouds of varying concentrations to electrical sparks of different energy levels. The test sample was placed in a sample cup at the base of an acrylic tube and was dispersed into a cloud by a blast of low pressure air. After a preset time delay to allow cloud formation, a low energy triggering spark was discharged between 2 electrodes to initiate discharge of a higher energy DC spark stored in a capacitor. A combustion event ("GO") was evidenced by observation of a flame accompanied by bursting of a full diameter paper rupture disc at the top of the tube. For a given energy level, tests were conducted at varying dust concentrations; if a "GO" event was obtained in 10 trials for any of the concentrations tested, the energy level was reduced and the tests repeated. This procedure was continued until and energy level was reached where no combustion events were observed in 10 trials for any of the concentrations tested. The MIE was then reported as being located between this energy level and the next highest energy level tested.

The LEL, LOC, and MIE values determined by these procedures are valid for atmospheric pressure and ambient temperature only.

Remark : Reliability: High because a scientifically defensible or guideline method was used.

Result : Lower Explosive Limit: 0.023 g/L
Limiting Oxygen Concentration: >12%
Minimum Ignition Energy: 20-50 mJ

27.12.2005 (9)

Remark : Additional References for Flammability:
27.12.2005 (8)

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	
Rate constant	:	cm^3/(molecule*sec)
Degradation	:	% after
Deg. product	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4

Method	:	Indirect Photolysis: Modeled. AOPWIN, v1.91 module of EPIWIN 3.11.
Remark	:	Reliability: Estimate based on known qualitative structure-activity relationships.
Result	:	The rate constant for reaction with OH radicals = 13.2668x10E-12 cm3/molecule-sec (24-hour day; 0.5x10E6 OH/cm3) yielding an estimated half-life of 29.024 hours.

27.12.2005 (23)

Type	:	water
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
Deg. product	:	
Method	:	other (measured)
Year	:	
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4

Method	:	Direct Photolysis: Inspection of chemical structure.
Remark	:	Reliability: Estimate based on known qualitative structure-activity relationships.
Result	:	Direct Photolysis: No Data, but inspection of the chemical structure indicates that sec-butyl urea does not contain structural fragments typically subject to aqueous photolysis.

27.12.2005 (14)

3.1.2 STABILITY IN WATER

Deg. product	:	
Method	:	other (calculated)
Year	:	
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4

Method	:	Modeled. HYDROWIN, v. 1.67 module of EPIWIN v3.05 (Syracuse Research Corporation). HYDROWIN estimates aqueous hydrolysis rate constants for the following chemical classes: esters, carbamates, epoxides, halomethanes and selected alkyl halides. HYDROWIN estimates acid- and base-catalyzed rate constants; it does NOT estimate neutral hydrolysis rate constants. The prediction methodology was developed for the U.S.

Environmental Protection Agency and is outlined in Mill et al., 1987.

Remark : Reliability: Estimated value based on accepted model.
Result : Concentration: No Data
Half-life: No value. The estimated rate of hydrolysis is extremely slow, beyond the typical range for quantitative model estimates.
% Hydrolyzed: No Data

27.12.2005 (27)

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : fugacity model level III
Media : other: Air, Water, Soil, and Sediments
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: Modeled
Year :

Method : Modeled.
Henry's Law Constant - HENRYWIN v. 3.10 module of EPIWIN v3.05 (Syracuse Research Corporation). Henry's Law Constant (HLC) is estimated by two separate methods that yield two separate estimates. The first method is the bond contribution method and the second is the group contribution method. The bond contribution method is able to estimate many more types of structures; however, the group method estimate is usually preferred (but not always) when all fragment values are available (Hine and Mookerjee, 1975; Meylan and Howard, 1993).

Log Koc - Calculated from log Kow by the Mackay Level III fugacity model incorporated into EPIWIN v3.05 [Syracuse Research Corporation] (Mackay, 1991; Mackay et al., 1996a, 1996b).

Environmental Distribution - Mackay Level III fugacity model, in EPIWIN v3.05 (Syracuse Research Corporation). Emissions (1000 kg/hr) to air, water, and soil compartments and the following input values (Mackay, 1991; Mackay et al., 1996a, 1996b):

Molecular Weight: 116.16
Henry's Law Constant: 1.87x10E-9 atm-m3/mole (HENRYWIN program)
Vapor Pressure: 0.00294 mm Hg (MPBPWIN program)
Melting Point : 171°C (user-entered)
Log Kow: 0.31 (KOWWIN program)
Soil Koc: 0.837 (calculated by Level III model)

Remark : Reliability: Estimated value based on accepted model.
Result : Distributions:

Air: 0.0594%

Water: 44.6%
Soil: 55.2%
Sediment: 0.0757%

Half-life:

Air: 29 hours
Water: 360 hours
Soil: 360 hours
Sediment: 1.44x10E3 hours

Adsorption Coefficient: Estimated log Koc = 0.84
Desorption: Not Applicable
Volatility: Not Applicable

27.12.2005 (16) (19) (20) (21) (22)

Remark : Data from this additional source support the study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

27.12.2005 (31)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	
Inoculum	:	activated sludge
Contact time	:	
Degradation	:	14 (±) % after 28 day(s)
Result	:	other: not ready biodegradable
Deg. product	:	
Method	:	OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO_2 evolution)"
Year	:	2005
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : The test substance was tested for ready biodegradability using the 28-day CO_2 evolution test for "ready biodegradation" according to OECD Guideline 301B in the version dated July 17, 1992. This test is also known as the Modified Sturm Test. The biological system used was secondary activated sludge from the Cecil County Maryland (USA) Publicly-Owned Treatment Works (POTW).

At 0, 2, 4, 7, 10, 14, 21, and 28 days the carbon dioxide (CO_2) trapped in the barium hydroxide was measured by titration of the residual hydroxide. The amount of CO_2 produced from the test substance (corrected for that derived from the blank inoculum) was expressed as a percentage of the total CO_2 that the test material could have theoretically produced based on carbon composition (ThCO_2). Test substances giving a result of greater than 60% yield of CO_2 (within 28 days) should be regarded as readily biodegradable. The level must be reached within 10 days of biodegradation exceeding 10% within the 28-day period of the test.

The positive control substance was sodium benzoate. The toxicity control was mineral medium with inoculum, test substance, and control substance.

Remark : Reliability: High because a scientifically defensible or guideline method was used.

Result : The test substance reached a maximum biodegradability of 14% by day 28. Greater than 60% biodegradability was not reached within 10 days of exceeding 10% biodegradation.

In the toxicity test, which included both the test substance and the positive control chemical in the same flask, the substances yielded greater than 25% biodegradation within 14 days.

The positive control substance was >60% biodegradable within 14 days, confirming that the inoculum was viable.

The test substance was considered not "ready biodegradable." The test substance was not inhibitory to microorganisms in the inoculum.

Test substance : sec-Butyl urea, purity 99.4%

07.03.2006 (13)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

Species :
Exposure period : at °C
Concentration :
Elimination :
Method : other: Modeled
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4

Method : Modeled. BCFWIN v. 2.4 module of EPINWINN v3.05 (Syracuse Research Corporation). BCFWIN estimates the bioconcentration factor (BCF) of an organic compound using the compound's log octanol-water partition coefficient (Kow) with correction factors based on molecular fragments (based on the reference below).

"Improved Method for Estimating Bioconcentration Factor (BCF) from Octanol-Water Partition Coefficient,"
SRC TR-97-006 (2nd Update), July 22, 1997; prepared for Robert S. Boethling, EPA-OPPT, Washington, DC, Contract No. 68-D5-0012; prepared by William M. Meylan, Philip H. Howard, Dallas Aronson, Heather Printup, and Sybil Gouchie, Syracuse Research Corp.

Remark : Reliability: Estimated value based on accepted model.

Result : BCF = 3.162 (log BCF = 0.500). This BCF value suggests that bioconcentration potential in aquatic organisms is low.

27.12.2005 (26)

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	other: Modeled
Species	:	other: Fish
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	3339
Method	:	other: Modeled by ECOSAR
Year	:	
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Reliability: Estimated value based on accepted model.
Result	:	Estimated 96-hour LC50 = 3339 mg/L (using log10 Kow of 0.31).

04.01.2006 (25)

Type	:	other: Modeled
Species	:	other: Fish (Modeled)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	372000
Method	:	other: Modeled by ECOSAR
Year	:	
GLP	:	no
Test substance	:	other TS
Remark	:	Reliability: Estimated value based on accepted model.
Result	:	Estimated 96-hour LC50 = 3.72x10E5 mg/L (using log10 Kow of -1.68).
Test substance	:	Isobutylidene diurea

04.01.2006 (25)

Type	:	static
Species	:	Salmo gairdneri (Fish, estuary, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
NOEC	:	1000
LC0	:	1000
LC50	:	> 1000
Limit test	:	
Analytical monitoring	:	no
Method	:	OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year	:	1986
GLP	:	no
Test substance	:	other TS
Remark	:	Reliability: Medium because a suboptimal study design for testing (nominal test concentrations) was used.
Result	:	The LC50 was calculated based on nominal test concentrations. The NOEC, LC0, and LC100 were 1000, 1000, and >1000 mg/L, respectively. No additional information was reported.
Test substance	:	Isobutylidene diurea, purity 88%

27.12.2005 (1)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	other: Modeled
Species	:	Daphnia sp. (Crustacea)

Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	3184
Method	:	other: Modeled by ECOSAR
Year	:	
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Reliability: Estimated value based on accepted model.
Result	:	Estimated 48-hour EC50 = 3184 mg/L (log10 Kow of 0.31).

04.01.2006 (25)

Type	:	other: Modeled
Species	:	Daphnia sp. (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	309000
Method	:	other: Modeled by ECOSAR
Year	:	
GLP	:	no
Test substance	:	other TS
Remark	:	Reliability: Estimated value based on accepted model.
Result	:	Estimated 48-hour EC50 = 3.09x10E5 mg/L (log10 Kow of -1.68).
Test substance	:	Isobutylidene diurea

04.01.2006 (25)

Type	:	static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC0	:	250
EC50	:	> 1000
EC100	:	> 500
Analytical monitoring	:	no
Method	:	Directive 84/449/EEC, C.2 "Acute toxicity for Daphnia"
Year	:	1987
GLP	:	no data
Test substance	:	other TS
Remark	:	Reliability: Medium because a suboptimal study design for testing (nominal test concentrations) was used.
Result	:	The EC50 was calculated based on nominal test concentrations. The 48-hour EC0 and EC100 were 250 and >500 mg/L, respectively. The 24-hour EC0, EC50, and EC100 were 500, >500, and >500 mg/L, respectively. No additional information was reported.
Test substance	:	Isobutylidene diurea, purity not reported

04.01.2006 (2)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	other algae: Modeled
Endpoint	:	
Exposure period	:	96 hour(s)
Unit	:	mg/l
EC50	:	1806
Method	:	other: Modeled by ECOSAR
Year	:	
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Remark	:	Reliability: Estimated value based on accepted model.
Result	:	Estimated 96-hour EC50 = 1806 mg/L (log10 Kow of 0.31).
04.01.2006		(25)
Species	:	other algae: Modeled
Endpoint	:	
Exposure period	:	96 hour(s)
Unit	:	g/l
EC50	:	156
Method	:	other: Modeled by ECOSAR
Year	:	
GLP	:	no
Test substance	:	other TS
Remark	:	Reliability: Estimated value based on accepted model.
Result	:	Estimated 96-hour EC50 = 1.56x10E5 mg/L (log10 Kow of -1.68).
Test substance	:	Isobutylidene diurea
04.01.2006		(25)
Species	:	Scenedesmus subspicatus (Algae)
Endpoint	:	other: Cell multipication inhibition
Exposure period	:	96 hour(s)
Unit	:	mg/l
EC50	:	> 500
Method	:	other
Year	:	1987
GLP	:	no data
Test substance	:	other TS
Method	:	DIN 38412 Part 9, "Scenedesmus-cell multiplication inhibition test, regulation of the inhibition effect of substances contained in water on green algae." No additional information was reported.
Remark	:	Reliability: Medium because a suboptimal study design for testing (nominal test concentrations) was used.
Result	:	The EC50 was calculated based on nominal test concentrations. The 96-hour EC20 was >500 mg/L. The 72 hour EC20 and EC50 were 500 and >500 mg/L, respectively. No additional information was reported.
Test substance	:	Isobutylidene diurea, purity not reported
04.01.2006		(2)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type	:	other: ALD
Value	:	7500 mg/kg bw
Species	:	rat
Strain	:	other: ChR-CD
Sex	:	male
Number of animals	:	12
Vehicle	:	peanut oil
Doses	:	670, 2250, 3400, 5000, 7500, 11,000, and 17,000 mg/kg
Method	:	other
Year	:	1964
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. The test substance was administered by intragastric intubation as a suspension in peanut oil in single doses of 670, 2250, 3400, 5000, 7500, 11,000, and 17,000 mg/kg to young adult male rats. Survivors were sacrificed 14 days later. Pathological examination was performed on the survivors.
Remark	:	Reliability: High because a scientifically defensible or guideline method was used.
Result	:	Mortality was 0/1, 0/1, 0/1, 0/2, 2/3, 0/2, and 1/2 at 670, 2250, 3400, 5000, 7500, 11,000, and 17,000 mg/kg, respectively. Mortality occurred within 2-3 days after dosing. Toxic signs observed at lethal doses included weight loss, red extremities, incoordination, lacrimation, prostration, and white precipitate from urine. Toxic signs at non-lethal doses were observed up to 2 days after dosing and included slight weight loss initially at 2250 mg/kg or higher; red extremities, unresponsiveness, and incoordination at 3400 mg/kg or higher; and white precipitate from the urine in 1 of 2 rats receiving 5000 mg/kg. At non-lethal doses, no pathologic changes that could be attributed to the test substance were observed in the tissues of rats that were sacrificed 14 days after treatment.
Test substance	:	sec-Butyl urea, purity 90%

27.12.2005 (6)

Remark	:	Data from this additional source support the study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

27.12.2005 (5)

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	
Dose	:	
Exposure time	:	
Comment	:	
Number of animals	:	4
Vehicle	:	
Result	:	moderately irritating
Classification	:	
Method	:	other
Year	:	1963
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Method : No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

Ten mg of the test substance, as powder, was sprinkled into the conjunctival sacs of 2 rabbit eyes. In addition, 0.1 mL of a 10% solution of the test substance in propylene glycol was instilled into the conjunctival sacs of another 2 rabbit eyes. One eye of each pair was irrigated with tap water 20 seconds after contact for a 1-minute interval. The other eye of each pair was not washed.

Remark : Reliability: High because a scientifically defensible or guideline method was used.

Result : In the eye that was treated with the powder and washed after treatment, mild corneal injury through 1 day, mild congestion in the iris on the day of treatment, moderate swelling of the conjuctiva at 4 hours, and mild conjunctival irritation through 1 day were observed. In the eye not washed after treatment, moderate localized corneal injury for 2 days, marked congestion of the iris through 1 day, marked conjunctival swelling at 4 hours, and moderate conjunctival irritation at 1 day were observed. The conjunctival irritation diminished through 4 days, and the eye was normal by 7 days.

In the eye that was treated with 0.1 mL 10% solution, no corneal injury, mild congestion through 1 day, and moderate conjunctival irritation on the day of treatment were observed in both treated eyes. The conjuctival irritation was mild through 1 day.

Applying the current EPA eye scoring criteria, sec-butyl urea would be classified as Toxicity Category III, moderate eye irritant, based on corneal involvement clearing in 7 days or less.

Test substance : sec-Butyl urea, purity 100%

27.12.2005

(4)

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Remark : Isolated Intermediate; Not a Required Endpoint

04.01.2006

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Bacterial reverse mutation assay
System of testing	:	Salmonella typhimurium TA98, TA100, TA1535, TA1537 and Escherichia coli WP2uvrA
Test concentration	:	0, 333, 667, 1000, 3333, 5000 µg/plate
Cycotoxic concentr.	:	
Metabolic activation	:	with and without
Result	:	negative
Method	:	OECD Guide-line 471
Year	:	2004
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : The procedures used in the test were based on the recommendations of the following guidelines:

U.S. EPA OPPTS 870.5100,

OECD Guideline 471,

European Commission Directive 2000/32/EC Annex 4D - B.13/14, No. L 136/57, and

MAFF Japan, Agriculture Chemicals Laws and Regulations, Japan (II), (59 NohSan Number 4200) (1985).

The test was performed in 2 phases. The first phase was the initial toxicity-mutation test, which was to establish the dose range for the main mutagenicity test, and to provide a preliminary mutagenicity evaluation. The second phase was the main mutagenicity test, which was used to evaluate and confirm the mutagenic potential of the test substance.

Dimethyl sulfoxide (DMSO) was chosen as the dosing vehicle based on the solubility of the test substance and compatibility with the target cells. Positive controls included benzo[a]pyrene, 4-nitroquinoline N-oxide, acridine mutagen ICR-191, sodium azide, 2-aminoanthracene, and 2-nitrofluorene. The positive controls were dissolved in DMSO, except for sodium azide and ICR-191, which were dissolved in sterile water. The positive controls were assumed to be stable during this assay and no evidence of instability was observed.

In the initial toxicity-mutation test, the maximum dose of the test substance evaluated was 5000 µg/plate. This dose was achieved using a concentration of 50 mg/mL and a 100 µL aliquot. The eight dose levels were 33.3, 66.7, 100, 333, 667, 1000, 3333, and 5000 µg/plate.

In the main mutagenicity test, the maximum dose of the test substance evaluated in this test was 5000 µg/plate. This dose was achieved using a concentration of 50 mg/mL and a 100 µL aliquot. The five dose levels were 333, 667, 1000, 3333, and 5000 µg/plate.

Remark : Reliability: High because a scientifically defensible or guideline method was used.

Result : The test substance was a clear solution in DMSO at the highest concentration, 50 mg/mL, tested in the study.

In the initial toxicity-mutation test, precipitate was not observed at any dose level. No appreciable toxicity was observed. Based on the findings of the

initial toxicity-mutation test, the maximum dose plated in the main mutagenicity test was 5000 µg/plate. No positive mutagenic response was observed in the initial toxicity-mutation test with any tester strain at any dose level in either the presence or absence of S9 activation.

In the main mutagenicity test, precipitate was not observed at any dose level. No appreciable toxicity was observed. No positive mutagenic responses were observed in the main mutagenicity test with any tester strain in either the presence or absence of S9 activation.

All criteria for a valid study were met. Under the conditions of this study, the test substance showed no evidence of mutagenicity in the Bacterial Reverse Mutation Test either in the presence or absence of Aroclor-induced rat liver S9.

Test substance : sec-Butyl urea, purity 99.4%
17.03.2006 (11)

Type : Chromosomal aberration test
System of testing : Human peripheral blood lymphocytes (HPBL)
Test concentration : 388, 775, and 1162 µg/mL
Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : OECD Guide-line 473
Year : 2004
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : The procedure used in the test were based on the recommendations of the following guidelines:

U.S. EPA OPPTS 870.5375,

OECD Guideline 473,

European Commission Directive 2000/32/EC Annex 4A-No. L 136, and

MAFF Japan, Agriculture Chemicals Laws and Regulations, Japan (II), (59 NohSan Number 4200) (1985).

The test substance was prepared in dimethyl sulfoxide (DMSO), as this vehicle was determined to be the solvent of choice based on solubility of the test substance and compatibility of the target cells. Dosing solutions were adjusted to compensate for the purity of the test substance. Positive controls included mitomycin C and cyclophosphamide. The positive controls were dissolved in sterile water. The positive controls were assumed to be stable during this assay, and no evidence of instability was observed.

Aliquots of the vehicle control and three test substance concentrations were taken to confirm dose concentrations and stability in the chromosome aberration study.

The maximum concentration tested in the preliminary toxicity assay based on the formula weight of the test substance was 10 mM (1162 µg/mL), the guidelined limit dose for this test system. The test substance formed a clear solution in DMSO at 500 mg/mL, the highest stock concentration used in the assay.

In the preliminary toxicity assay, HPBL cells were treated for 4 and 20 hours in the non-activated test system and for 4 hours in the S9 activated test system. The cells were exposed to 9 concentrations of the test

substance ranging from 6 to 1162 µg/mL (10 mM), as well as vehicle controls. The test substance concentrations for the chromosome aberration assay were selected based on an assessment of the potential reduction in the mitotic index in the treated cultures relative to the vehicle control.

In the chromosome aberration assay, the HPBL cells were treated for 4 and 20 hours in the non-activated test system and for 4 hours in the S9 activated test system. The cells were harvested 20 hours after initiation of the treatment.

Cytogenetic evaluations were conducted at 388, 775, and 1162 µg/mL for all three testing conditions.

Remark : Reliability: High because a scientifically defensible or guideline method was used.

Result : Target concentrations were verified, and the test substance was stable for the duration of the dosing period.

In the preliminary toxicity assay, at concentrations of 1162 µg/mL or lower, no visible precipitate was observed in the treatment medium. The pH and osmolality of the highest test substance concentration in media was not significantly different from the vehicle control either in the absence or presence of S9. Substantial toxicity (at least a 50% reduction in mitotic index relative to the solvent control) was observed at 1162 µg/mL in the 4-hour activated testing condition. In the 4-hour and 20-hour non-activated testing conditions, substantial mitotic inhibition relative to the vehicle control was not observed at any concentration level. Based on these findings, the concentrations chosen for the chromosome aberration assay ranged from 97 to 1162 µg/mL for all three testing conditions.

In the chromosome aberration assay, the test substance was soluble in DMSO at all concentrations tested. No visible precipitate was observed in the treatment medium at the beginning or end of the treatment period at any concentration (1162 µg/mL or lower) in any testing condition. Substantial toxicity (at least 50% reduction in mitotic index relative to the solvent control) was not observed at any concentration level in any testing condition. Selection of doses for microscopic analysis was therefore based on the guidelined 10 mM limit dose for this test system.

The percentage of cells with structural or numerical aberrations in the test substance-treated groups was not significantly increased above that of the solvent control at any concentration.

All criteria for a valid study were met. Under the conditions of this study, the test substance did not induce structural or numerical chromosome aberrations in the in vitro mammalian chromosome aberration test in human peripheral blood lymphocytes in the non-activated or S9 activated test systems.

Test substance : sec-Butyl urea, purity 99.4%

17.03.2006 (10)

5.6 GENETIC TOXICITY 'IN VIVO'

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Remark	:	Although no data for sec-butylurea exists, data available for structurally similar compounds (isobutylenediurea, urea, 1-ethylurea, 1-methylurea, and 1,3-dimethylurea) are summarized.
04.01.2006		
Species	:	rat
Sex	:	female
Strain	:	Wistar
Route of admin.	:	gavage
Exposure period	:	Days 6-15 post-coitum; Cesarean section on Day 20 post coitum
Frequency of treatm.	:	Daily
Duration of test	:	20 days
Doses	:	0, 100, 400, 1000 mg/kg
Control group	:	yes
NOAEL maternal tox.	:	1000
NOAEL teratogen.	:	1000
Method	:	OECD Guide-line 414 "Teratogenicity"
Year	:	1997
GLP	:	yes
Test substance	:	other TS

Method :

The procedure used in the test was based on the recommendations of the following guidelines:

Commission Directive 87/302/EEC of 18 November 1987 adapting to technical progress for the 9th time Council Directive 67/548/EEC;

OECD Guideline No. 414;

EPA/FIFRA Pesticide Assessment Guidelines, Subdivision F, NTIS, §83-3, November 1984; and

Testing Guidelines for Toxicology Studies, Japan/MAFF, 1985.

A re-analysis of the stability of the test substance was performed on completion of the study. Analytical verifications of the stability of the IBDU suspensions in 0.5% aqueous carboxymethyl cellulose solution for up to 3 hours after preparation were performed. For verification of the concentrations, samples of the suspensions were twice analyzed by HPLC during the study period. At the beginning of the dosing period, samples were also used to verify the homogeneity of the 100 and 1000 mg/kg/day concentrations.

One to 4 female rats (65-74 days old; mean body weight of approximately 225 g) were mated with 1 male. The day on which sperm was detected in the vaginal smear was defined as Day 0, and the following day as day 1 post-coitum (p.c.). Suspensions of IBDU in 0.5% aqueous carboxymethyl cellulose solution were freshly prepared before oral administration at a volume of 10 mL/kg body weight. All dams were weighed on days 0, 1, 3, 6, 8, 10, 13, 15, 17, and 20 p.c. With the exception of day 0, food consumption was recorded on the same days as body weight. On day 20 p.c. the dams were killed and given a gross autopsy. Body weight changes were determined and the corrected body weight gains were calculated. Intact uterine weight, number of corpora lutea, and number of implants (differentiated into live fetuses, dead implants, early and late resorptions, and dead fetuses) were recorded. The conception rate and pre- and post-implantation losses were calculated.

Fetuses were weighed and examined for external alterations, and sex was determined. Soft tissue examinations were performed on approximately 50% of fetuses after fixation in Bouin's solution, according to the method of Barrow and Taylor, 1969. Fetuses that did not receive a soft tissue examination were fixed in ethyl alcohol, stained, and examined for skeletal alterations.

Dunnett's test was used for statistically evaluating food consumption, body weight, body weight changes, corrected body weight gain, intact uterine weight, fetal and placental weights, the number of corpora lutea, implants, resorptions, live fetuses, and pre-or post-implantation losses. Fisher's exact test was used to evaluate the conception rate, maternal mortality, and all fetal findings.

Remark : Reliability: High because a scientifically defensible or guideline method was used.

Result : The content of active ingredient was 90% prior to the beginning of the study. The re-analysis on its completion confirmed the tentative conclusion the suspensions were stable over a period of 3 hours at room temperature. It was also concluded that the prepared concentrations and the homogenous distribution of the test substance in the carrier were correct.

Pregnancy ratios were 23/25, 22/25, 22/25, and 24/25 at 0, 100, 400, and 1000 mg/kg/day, respectively. There were no mortalities or early deliveries observed at any dose level. No test substance-related effects on body weight, body weight gain, corrected body weight gain, food consumption, clinical signs, mean uterine weights, or gross pathological findings were observed. No test substance-related differences in conception rate, mean number of corpora lutea, implantation sites, values calculated for pre- and post implantation loss, number of resorptions, or viable fetuses were observed. There was no effect on sex ratio, mean placental weight, or mean fetal weight. A summary of other reproductive outcomes (means/litter) are provided below [0; 100; 400; and 1000 ppm groups, respectively]:

Corpora Lutea: 16.8; 15.5; 15.8; and 15.7

Implantations: 15.7; 14.5; 14.3; and 14.4

% Pre-implantation loss: 6.7; 6.3; 10.0; and 9.8

Dead implants: 0.8; 1.0; 1.1; and 0.9

% Post-implantation loss: 5.2; 7.3; 8.6; and 6.1

Total No. of Live Fetuses: 14.9; 13.6; 13.2; and 13.5

Mean Fetal Weight (g): 3.8; 3.9; 4.0; and 3.9

Sex Ratio (male:female): 52.8:47.2; 53.2:46.8; 53.3:46.7; and 48.3:51.7

Increased incidences of 2 skeletal malformations were unrelated to treatment. The overall malformation rate of the fetal skeletons was statistically significantly increased only in the 100 and 400 mg/kg/day dose groups. The differences observed between these treatment groups and the control fetuses were judged incidental since the frequency of dumbbell-shaped thoracic vertebral body/bodies (asymmetrical) and/or bipartite sternebra(e) with dislocated ossification centers was unusually low in the concurrent control group. Moreover, the slightly, albeit statistically significantly increased number of fetuses at 100 mg/kg/day with skeletal variations was interpreted as being spontaneous due to the lack of a dose-response relationship. Concerning fetal external, soft tissue, and skeletal findings, all differences observed between the control and the treated

groups appeared without a clear dose-response relationship and were therefore judged as being without biological relevance. All the relevant findings occurred at incidences that were all within the range of historical control data.

A summary of statistically significant fetal anomalies are provided below. Data are presented as number of fetuses (litters) affected [0; 100; 400; and 1000 ppm groups, respectively]:

Skeletal, Number examined: 177(23); 156(22); 151(22); and 168(24)

Thoracic vertebral body/bodies dumbbell shaped (asymmetrical): 0(0); 5(4); 10(7); and 5(4)

Sternebra(e) bipartite, ossification centers dislocated: 0(0); 1(1); 4(3); and 2(2)

Total fetal skeletal malformations: 2(2); 9(7); 15(10); and 7(5)

Thus there was no indication of IBDU-induced embryo/fetotoxicity or teratogenicity in Wistar rats, even at the highest dose. The NOAEL for the maternal and developing organism was 1000 mg/kg/day.

Test condition : There were 25 rats per group.
Test substance : Isobutylidenediurea, purity 90%
04.01.2006 (15)

Species : other: Rats and mice
Sex : female
Strain : other: See Method Section for details
Route of admin. : gavage
Exposure period : Rats: Gestation Day 12 and Mice: Gestation Day 10
Frequency of treatm. : Single oral dose
Duration of test : 18-20 days
Doses : Rats: 2000 mg/kg and Mice: 1000 and 2000 mg/kg
Control group : yes
Method : other
Year :
GLP : no data
Test substance : other TS

Method : Wistar rats and ICR mice at 15 and 8 weeks of age, respectively, were used. They were housed in a controlled environment of 24±1°C and 55±5% relative humidity, maintained on laboratory chow, and given tap water ad libitum. Four female rats and three female mice per dose level were paired overnight with a male, and were examined the following morning for the presence of vaginal plug (Day 0 of gestation).

Aqueous solutions of the test substances were prepared and given orally to female rats by intubation on day 12 of pregnancy, and on day 10 of pregnancy to female mice. Female rats and mice were killed on days 20 and 18 of pregnancy, respectively. The number of implants and live and dead fetuses were counted. Live fetuses were individually weighed and examined for gross abnormalities, and then divided into 2 groups. One group (derived from the right uterine horn) was processed for skeletal examinations. The other group was fixed in Bouin's and examined for visceral anomalies.

Differences in numbers of implants, live fetuses, and fetal body weights were analyzed by the Student's t test. The litter was considered the experimental unit. Differences in resorption and malformation incidences, assessed on the basis of number of affected fetuses, were analyzed by the Chi-square test.

Remark	:	Reliability: Medium because a suboptimal study design was used.
Result	:	Urea had no observable effect on fetal development in either rats or mice. Fetal survival and fetal weights were comparable to controls.
Test condition	:	There were 4 rats and 3 mice per level.
Test substance	:	Urea, purity not reported

04.01.2006 (18) (33)

Species	:	rat
Sex	:	female
Strain	:	Wistar
Route of admin.	:	gavage
Exposure period	:	14 days starting on the 6th day after last estrus
Frequency of treatm.	:	2 times daily, half of the dose each time
Duration of test	:	
Doses	:	5000 mg/kg
Control group	:	no data specified
Method	:	other: No data
Year	:	1969
GLP	:	no data
Test substance	:	other TS

Method	:	No data
Remark	:	Reliability: Medium because a suboptimal study design was used.
Result	:	Maternal toxicity included indications of apathy and loss of appetite. Plasma urea 1 hour post application was 1000 mg%, and 12 hours post application was 100 mg%. The young animals were examined before 48 hours post partum. Except for a slightly reduced birth weight no effects were found, especially on the kidneys there were no specific findings.
Test substance	:	Urea, purity not reported

04.01.2006 (30)

Species	:	other: Rats and mice
Sex	:	female
Strain	:	other: See Method Section for details
Route of admin.	:	gavage
Exposure period	:	Rats: Gestation day 12 and Mice: Gestation day 10
Frequency of treatm.	:	Single oral dose
Duration of test	:	
Doses	:	2000 mg/kg
Control group	:	yes
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	other TS

Method : Rats and mice at 15 and 8 weeks of age, respectively, were used. They were housed in a controlled environment of 24±1°C and 55±5% relative humidity, maintained on laboratory chow, and given tap water ad libitum. Female rats and mice were paired overnight with a male, and were examined the following morning for the presence of vaginal plug (Day 0 of gestation).

Aqueous solutions of the test substances were prepared and given orally to female rats by intubation on day 12 of pregnancy, and on day 10 of pregnancy to female mice. Urea and thiourea were used as negative controls. Female rats and mice were killed on days 20 and 18 of pregnancy, respectively. The number of implants and live and dead fetuses were counted. Live fetuses were individually weighed and examined for gross abnormalities, and then divided into 2 groups. One group (derived from the right uterine horn) was processed for skeletal examinations. The other group was fixed in Bouin's and examined for visceral anomalies.

Differences in numbers of implants, live fetuses, and fetal body weights were analyzed by the Student's t test. The litter was considered the experimental unit. Differences in resorption and malformation incidences, assessed on the basis of number of affected fetuses, were analyzed by the Chi-square test.

Remark : Reliability: Medium because a suboptimal study design was used.
Result : Methylurea had no observable effect on fetal development in either rats or mice. Fetal survival and fetal weights were comparable to controls.
Test condition : There were 6 rats and 10 mice in the groups.
Test substance : Methylurea, purity not reported
04.01.2006 (18) (33)

Species : mouse
Sex : female
Strain : ICR
Route of admin. : oral feed
Exposure period : Gestation days 6-15
Frequency of treatm. : Ad libitum
Duration of test :
Doses : 0, 6000 mg/kg
Control group : yes
Method : other
Year : 1988
GLP : no data
Test substance : other TS

Method : Pregnant mice were given food, which contained ethylurea. The dams were killed on gestational day 18 and examined for maternal and embryo toxicity.
Remark : Reliability: Medium because limited study information was available.
Result : Ethylurea had no effect on maternal reproduction and fetal development. No further details were provided.
Test substance : Ethylurea, purity not reported
04.01.2006 (29)

Species : other: Rats and mice
Sex : female
Strain : other: See Method Section for details
Route of admin. : gavage
Exposure period : Rats: Gestation day 12 and Mice: Gestation day 10
Frequency of treatm. : Single oral dose
Duration of test :
Doses : 2000 mg/kg
Control group : yes
Method : other
Year :
GLP : no data
Test substance : other TS

Method : Rats and mice at 15 and 8 weeks of age, respectively, were used. They were housed in a controlled environment of 24±1°C and 55±5% relative humidity, maintained on laboratory chow, and given tap water ad libitum. Female rats and mice were paired overnight with a male, and were examined the following morning for the presence of vaginal plug (Day 0 of gestation).

Aqueous solutions of the test substances were prepared and given orally to female rats by intubation on day 12 of pregnancy, and on day 10 of pregnancy to female mice. Urea and thiourea were used as negative controls. Female rats and mice were killed on days 20 and 18 of pregnancy, respectively. The number of implants and live and dead

fetuses were counted. Live fetuses were individually weighed and examined for gross abnormalities, and then divided into 2 groups. One group (derived from the right uterine horn) was processed for skeletal examinations. The other group was fixed in Bouin's and examined for visceral anomalies.

Differences in numbers of implants, live fetuses, and fetal body weights were analyzed by the Student's t test. The litter was considered the experimental unit. Differences in resorption and malformation incidences, assessed on the basis of number of affected fetuses, were analyzed by the Chi-square test.

Remark : Reliability: Medium because a suboptimal study design was used.
Result : Ethylurea had no observable effect on fetal development in either rats or mice. Fetal survival and fetal weights were comparable to controls. In the group of mice treated with ethylurea, a lower value in the number of implants led to a significant decrease n the number of live fetuses.
Test condition : There were 6 rats and 12 mice per group.
Test substance : Ethylurea, purity not reported
04.01.2006 (18) (33)

Species : rat
Sex : female
Strain : Wistar
Route of admin. : gavage
Exposure period : Days 6-15 of gestation
Frequency of treatm. : Once daily
Duration of test :
Doses : 0, 30, 100, and 200 mg/kg
Control group : yes
NOAEL maternal tox. : 30 mg/kg bw
NOAEL teratogen. : 30 mg/kg bw
Method : OECD Guide-line 414 "Teratogenicity"
Year : 1993
GLP : yes
Test substance : other TS

Remark : Reliability: High because a scientifically defensible or guideline method was used.
Result : Maternal toxicity was observed at 100 mg/kg or higher, as evidenced by reduced body weight and food consumption. At 200 mg/kg, clearly reduced placenta weight and fetal body weight were observed. Fetuses in this dose group had increased incidences of hydroureter and skeletal retardation. At 100 mg/kg an increased incidence of hydroureter in the fetuses was observed. No effects were observed in the dams or fetuses at 30 mg/kg. The maternal and developmental NOEL was 30 mg/kg.
Test substance : 1,3-Dimethylurea, purity not reported
04.01.2006 (3)

Species : other: Rats and mice
Sex : female
Strain : other: See Method Section for details
Route of admin. : gavage
Exposure period : Rats: Gestation day 12 and Mice: Gestation day 10
Frequency of treatm. : Single oral dose
Duration of test :
Doses : 2000 mg/kg
Control group : yes
Method : other
Year :
GLP : no data
Test substance : other TS

Method : Rats and mice at 15 and 8 weeks of age, respectively, were used. They were housed in a controlled environment of 24±1°C and 55±5% relative humidity, maintained on laboratory chow, and given tap water ad libitum. Female rats and mice were paired overnight with a male, and were examined the following morning for the presence of vaginal plug (Day 0 of gestation).

Aqueous solutions of the test substances were prepared and given orally to female rats by intubation on day 12 of pregnancy, and on day 10 of pregnancy to female mice. Urea and thiourea were used as negative controls. Female rats and mice were killed on days 20 and 18 of pregnancy, respectively. The number of implants and live and dead fetuses were counted. Live fetuses were individually weighed and examined for gross abnormalities, and then divided into 2 groups. One group (derived from the right uterine horn) was processed for skeletal examinations. The other group was fixed in Bouin's and examined for visceral anomalies.

Differences in numbers of implants, live fetuses, and fetal body weights were analyzed by the Student's t test. The litter was considered the experimental unit. Differences in resorption and malformation incidences, assessed on the basis of number of affected fetuses, were analyzed by the Chi-square test.

Remark : Reliability: Medium because a suboptimal study design was used.

Result : 1,3-Dimethylurea caused only a decrease in the weight of rat fetuses. In the mouse fetuses, it was observed to produce an increase in fetal resorptions and a decrease in the fetal weights. It also induced cleft palate and fusion of caudal vertebrae in 8 fetuses from 5 dams and in 12 fetuses from 8 dams, respectively.

Test condition : There were 6 rats and 11 mice per group.

Test substance : 1,3-Dimethylurea, purity not reported

04.01.2006 (18) (33)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

Remark : Isolated Intermediate; Not a Required Endpoint

04.01.2006

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

5.11 ADDITIONAL REMARKS

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

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10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT